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Modified Form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)	Application Number	09/834,778
	Filing Date	April 12, 2001
	First Named Inventor	Silver
	Group Art Unit	1636
	Examiner Name	Pappu
	Attorney Docket Number	20363-011

U.S. PATENT DOCUMENTS							
Exam Initials	Cite No.	U.S. Patent Document No.	Issue Date	Name of Patentee(s) or Applicant(s)	Class	Sub Class	Filing Date If Appropriate
	A1	4,959,317	09/25/90	Sauer			
	A2	5,629,159	05/13/97	Anderson			
	A3	5,885,836	03/23/99	Wahl et al.			
	A4	6,025,192	02/15/00	Beach et al.			
	A5	6,140,129	10/31/00	Cox et al.			
	A6	6,175,058	01/16/01	Baszczynski et al.			
	A7	6,200,800	03/13/01	Choulika et al.			

FOREIGN PATENT DOCUMENTS						
Exam Initials	Cite No.	Foreign Patent Document Office Number	Name of Patentee(s) or Applicant(s)	Date of Publication	Translation Yes No	
	B1	DE 195 30 412	Melchner et al. English Abstract	02/20/97		X

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS		
Exam Initials	Cite No.	Name of Author, Title (when appropriate), Publication, Volume, Page(s), Date, Etc.
	C1	Abremski et al. (1983). "Studies on the Properties of P1 Site-Specific Recombination: Evidence for Topologically Unlinked Products Following Recombination" <i>Cell</i> 32: 1301-1311.
	C2	Abremski and Hoess (1984). "Bacteriophage P1 Site-specific Recombination" <i>J. Biol. Chem.</i> 259(3): 1509-1514.
	C3	Amin et al. (1990). "Synaptic Intermediates Promoted by the FLP Recombinase" <i>J. Mol. Biol.</i> 214: 55-72.
	C4	Buchholz et al. (1998). "Improved properties of FLP recombinase evolved by cycling mutagenesis" <i>Nat. Biotechnol.</i> 16(7): 657-662.
	C5	Cox (1989). "DNA Inversion in the 2µm Plasmid of <i>Saccharomyces cerevisiae</i> " <i>Mobile DNA</i> . pages 661-670. (American Soc. of Microbiology, Wash., DC).
	C6	Craig (1988). "The Mechanism of Conservative Site-Specific Recombination" <i>Ann. Rev. Genet.</i> 22: 77-105
	C7	Cregg and Madden (1989). "Use of site-specific recombination to regenerate selectable markers" <i>Mol. Gen. Genet.</i> 219: 320-323.
	C8	Echols (1990). "Nucleoprotein Structures Initiating DNA Replication, Transcription, and Site-specific Recombination" <i>J. Biol. Chem.</i> 265: 14697-14700.
	C9	Falco et al. (1982). "Genetic Properties of Chromosomally Integrated 2µ Plasmid DNA In Yeast" <i>Cell</i> 29:573-584.
	C10	Flanagan and Fennewald (1989). "Analysis of Inhibitors of the Site-specific Recombination Reaction Mediated by Tn3 Resolvase" <i>J. Mol. Biol.</i> 206: 295-304.
	C11	Glasgow et al. (1989). "DBA-binding Properties of the Hin Recombinase" <i>J. Biol. Chem.</i> 264(17): 10072-10082.
	C12	Golic and Lindquist (1989). "The FLP Recombinase of Yeast Catalyzes Site-Specific Recombination in the Drosophila Genome" <i>Cell</i> 59: 499-509.
	C13	Gossen and Bujard (1992). "Tight control of gene expression in mammalian cells by tetracycline-responsive promoters" <i>Proc. Natl. Acad. Sci USA</i> 89: 5547-5551.

OTHER PRIOR ART - NON-PATENT LITERATURE DOCUMENTS		
Exam Initials	Cite No.	Name of Author, Title (when appropriate), Publication, Volume, Page(s), Date, Etc.
	C14	Hafter and Bickle (1988). "Enhancer-independent mutants of the <i>Cin</i> recombinase have a relaxed topological specificity" <i>EMBO J.</i> <u>7</u> (12): 3991-3996.
	C15	Hamilton and Abremski (1984). "Site-specific Recombination by the Bacteriophage P1 <i>lox</i> -Cre system" <i>J. Mol. Biol.</i> <u>178</u> : 481-486.
	C16	Hoess et al. (1982). "P1 site-specific recombination: Nucleotide sequence of the recombining sites" <i>Proc. Natl. Acad. Sci. USA</i> <u>79</u> : 3398-3402.
	C17	Hoess et al. (1984). "The Nature of the Interaction of the P1 Recombinase Cre with the Recombining Site <i>loxP</i> " <i>Cold Spring Harbor Symp. Quant. Biol.</i> <u>49</u> : 761-768.
	C18	Hoess et al. (1986). "The role of the <i>loxP</i> spacer region in P1 site-specific recombination" <i>Nucleic Acids Res.</i> <u>14</u> (5): 2287-2300.
	C19	Hubner et al. (1989). "Bent DNA is Needed for Recombinational Enhancer Activity in the Site-Specific Recombination System <i>Cin</i> of Bacteriophage P1" <i>J. Mol. Biol.</i> <u>205</u> : 493-500.
	C20	Hunger-Bertling et al. (1990). "Short DNA fragments induce site-specific recombination in mammalian cells" <i>Mol. Cell. Biochem.</i> <u>92</u> : 107-116.
	C21	Kellendonk et al. (1996). "Regulation of Cre recombinase activity by the synthetic steroid RU 486" <i>Nucleic Acids Res.</i> <u>24</u> (8): 1404-1411.
	C22	Kilby et al. (1993). "Site-specific recombinases: tools for genome engineering" <i>Trends Genet.</i> <u>9</u> : 413-421.
	C23	Kuhn et al. (1995). "Inducible Gene Targeting in Mice" <i>Science</i> <u>269</u> : 1427-1429.
	C24	Lee and Saito (1998). "Role of nucleotide sequences of <i>loxP</i> spacer region in Cre-mediated recombination" <i>Gene</i> <u>216</u> : 55-65.
	C25	Lewandowski and Martin (1997). "Cre-mediated chromosome loss in mice" <i>Nat. Genet.</i> <u>17</u> : 223-225.
	C26	Mercier et al. (1990). "Structural and Functional Characterization of <i>tnpI</i> , a Recombinase Locus in Tn21 and Related β -Lactamase Transposons" <i>J. Bacteriol.</i> <u>172</u> (7): 3745-3757.
	C27	Malynn et al. (1988). "Thesoid Defect Affects the Final Step of the Immunoglobulin VDJ Recombinase Mechanism" <i>Cell</i> <u>54</u> : 453-460.
	C28	Matsuzaki et al. (1990). "Chromosome Engineering in <i>Saccharomyces cerevisiae</i> by Using a Site-specific Recombination System of a Yeast Plasmid" <i>J. Bacteriol.</i> <u>172</u> (2): 610-618.
	C29	Metzger et al. (1995). "Conditional site-specific recombination in mammalian cells using a ligand-dependent chimeric Cre recombinase" <i>Proc. Natl. Acad. Sci. USA</i> <u>92</u> : 6991-6995.
	C30	Muller (1999). "Ten years of gene targeting: targeted mouse mutants, from vector design to phenotype analysis" <i>Mech. Dev.</i> <u>82</u> : 3-21.
	C31	Nagy (2000). "Cre Recombinase: The Universal Reagent for Genome Tailoring" <i>Genesis</i> <u>26</u> : 99-109.
	C32	Parsons et al. (1990). "Functional Analysis of Arg-308 Mutants of Flp Recombinase" <i>J. Biol. Chem.</i> <u>265</u> (8): 4527-4533.
	C33	Poyart-Salmeron et al. (1989). "Molecular characterization of two proteins involved in the excision of the conjugative transposon Tn1545: homologies with other site-specific recombinases" <i>EMBO J.</i> <u>8</u> (8): 2425-2433.
	C34	Rajewsky et al. (1996). "Perspective Series: Molecular Medicine in Genetically Engineered Animals" <i>J. Clin. Invest.</i> <u>98</u> (3): 600-603.
	C35	Ramirez-Solis et al. (1995). "Chromosome engineering in mice" <i>Nature</i> <u>378</u> : 720-724.
	C36	Rossant and McMahon (1999). "Cre'-ating mouse mutants - a meeting review on conditional mouse genetics" <i>Genes Dev.</i> <u>13</u> : 142-145.
	C37	Sato et al. (1990). "The <i>cisA</i> Cistron of <i>Bacillus subtilis</i> Sporulation Gene <i>spoIVC</i> Encodes a Protein Homologous to a Site-Specific Recombinase" <i>J. Bacteriol.</i> <u>172</u> (2): 1092-1098.
	C38	Sauer (1992). "Identification of Cryptic <i>lox</i> Sites in the Yeast Genome by Selection for Cre-mediated Chromosome Translocations that Confer Multiple Drug Resistance" <i>J. Mol. Biol.</i> <u>223</u> : 911-928.
	C39	Sauer (1998). "Inducible Gene Targeting in Mice Using the Cre/ <i>lox</i> System" <i>Methods</i> <u>14</u> : 381-392.
	C40	Sauer and Henderson (1988). "Site-specific DNA recombination in mammalian cells by the Cre recombinase of bacteriophage P1" <i>Proc. Natl. Acad. Sci. USA</i> <u>85</u> : 5166-5170.
	C41	Schlake and Bode (1994). "Use of Mutated FLP Recognition Target Sites for the Exchange of Expression Cassettes at Defined Chromosomal Loci" <i>Biochem.</i> <u>33</u> : 12746-12751.

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS		
Exam Initials	Cite No.	Name of Author, Title (when appropriate), Publication, Volume, Page(s), Date, Etc.
	C42	Schmidt et al. (2000). "Illegitimate Cre-dependent chromosome rearrangements in transgenic mouse spermatids" <i>Proc. Natl. Acad. Sci. USA</i> <u>97</u> (25): 13702-13707.
	C43	Schwartz and Sadowski (1989). "FLP Recombinase of the 2 μ m Circle Plasmid of the <i>Saccharomyces cerevisiae</i> Bends Its DNA Target" <i>J. Mol. Biol.</i> <u>205</u> : 647-658.
	C44	Stark et al. (1989). "Site-Specific Recombination by Tn3 Resolvase: Topological Changes in the Forward and Reverse Directions" <i>Cell</i> <u>58</u> : 779-790.
	C45	Sternberg and Hamilton (1981). "Bacteriophage P1 Site-specific Recombination" <i>J. Mol. Biol.</i> <u>150</u> : 467-486.
	C46	Sternberg et al. (1986). "Bacteriophage P1 cre Gene and its Regulatory Region" <i>J. Mol. Biol.</i> <u>187</u> : 197-212.
	C47	St. Onge et al. (1996). "Temporal control of the Cre recombinase in transgenic mice by a tetracycline responsive promoter" <i>Nucleic Acids Res.</i> <u>24</u> (19): 3875-3877.
	C48	Thyagarajan et al. (2000). "Mammalian genomes contain active recombinase recognition sites" <i>Gene</i> <u>244</u> : 47-54.
	C49	de Villartay et al. (1988). "Deletion of the human T-cell receptor δ -gene by a site-specific recombination" <i>Nature</i> <u>335</u> : 170-174.
	C50	Weisberg and Landy (1983). "Site-specific Recombination in Phage Lambda" <i>Lambda II</i> . Pages 211-250. (Cold Springs Harbor Press)
	C51	Zhang et al. (1996). "Inducible site-directed recombination in mouse embryonic stem cells" <i>Nucleic Acids Res.</i> <u>24</u> (4): 542-548.
	C52	Russ et al. (1996). "Self-Deleting Retrovirus Vectors for Gene Therapy" <i>J. Virol.</i> <u>70</u> (8): 4927-4932.
	C53	Bunting et al. (1999). "Targeting genes for self-excision in the germ line" <i>Genes & Development</i> <u>13</u> (12): 1524-1528.
	C54	Choulika et al. (1996). "Transfer of Single Gene-Containing Long Terminal Repeats into the Genome of Mammalian Cells by a Retroviral vector Carrying the cre Gene and the loxP Site" <i>J. Virol.</i> <u>70</u> (3): 1792-1798.
	C55	Silver et al. (2001). "Self-Excising Retroviral Vectors Encoding the Cre Recombinase Overcome Cre-Mediated Cellular Toxicity" <i>Mol. Cell</i> <u>8</u> (1): 233-243.
	C56	International Search Report for PCT/US 01/12193. Mailed on November 28, 2001.

* a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. _____, filed _____, and relied upon for an earlier filing date under 35 U.S.C. §120 (continuation, continuation-in-part, and divisional applications).

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